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Original article

Colon Polyps in Childhood: Increased Mucosal Eosinophilia in Juvenile Polyps

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SUMMARY

Aim: To study colon polyps in childhood, classify them according to histology and investigate the significance of colonic mucosal eosinophilia as a possible factor in the pathogenesis of juvenile polyps. Methods: The records of 128 consecutive children with colon polyps diagnosed in our endoscopy unit from 1987 to 2007 were reviewed. Polyps were classified according to location and histological characteristics. The association between juvenile polyps and mucosal eosinophilia was studied. Results: The mean age for polyp diagnosis was 5±3.2 years. One-hundred and twenty-one children (94.53%) had a solitary juvenile polyp, 3 juvenile polyposis coli (3.34%), 3 (3.34%) multiple adenomatous colonic polyps, and one Peutz-Jeghers syndrome. Polyps were more prevalent in the-rectosigmoid. Simultaneous colonic biopsies were taken in 92 children. Among children with juvenile polyps 73 (82.95%) had prominent eosinophilic infiltration of the polyp and 67 children (76.14%) eosinophilic infiltration of the colonic mucosa. Eosinophilia correlated inversely with patient's age ($p<0.01$) and positively with the size of the polyp ($p<0.05$). Conclusions: In our series most colonic polyps in children are juvenile and solitary. The prominent eosinophilic infiltration of both the polyp and the adjacent colonic mucosa may support an allergic aetiology in the pathogenesis of colon juvenile polyps.

Key words: children, colon polyps, mucosal eosinophilia

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INTRODUCTION

Colon polyps are common in children. The histologic type of the polyp is important in determining its potential for cancer development.[1] The vast majority of childhood polyps (75-90%) are classified as juvenile (JP) also known as "retention," or "hamartomatous" polyps. JP occur singly or in clusters of two to four, typically at the rectosigmoid and are usually pendunculated.[2,3] The age of onset ranges from 2 to 8 years with a peak between 3-4 years, and they are present in 3-4% of population aged below 21 years, usually in a sporadic manner. The aetiology of JP still remains largely unknown and no data exist concerning the role of eosinophils on polyp formation in childhood. In the present study we reviewed the histological characteristics of all colon polyps detected during the last two decades in our endoscopy unit. In addition, we aimed to investigate the significance of eosinophilic infiltration of colonic mucosa and its possible pathogenetic impact on the development of juvenile polyps.

MATERIALS AND METHODS

Over a 21 year period (1987-2007) all children admitted to Aghia Sophia Children's Hospital, a major referral center, with lower gastrointestinal bleeding due to colonic polyps were ascertained by review of endoscopic and histology records, following approval of the local Ethical Committee. During the study period, both endoscopy and histology were performed by the same endoscopists (ER, JP, GG) and histopathologist (CV). According to our protocol for the investigation of colonic polyps, all children

had total colonoscopy and at least two biopsies were taken from all parts of the large bowel (caecum, ascending, transverse, descending, sigmoid, rectum) in most of the children, while in the case of polyp two more biopsies from the surrounding area were taken. In addition, gastroscopy was performed in patients with juvenile polyposis coli (JPC), a positive family history for familial adenomatous polyposis (FAP), or Peutz-Jeghers syndrome. Polyps were classified according to their size in those <1cm, between 1 and 2 cm, between 2and 3cm and above 3 cm. Significant eosinophilic infiltration in the lamina propria of colonic mucosa was defined as the detection of >20 eosinophils/high power field. Statistical analysis was carried out through multiple regression analysis using SPSS (version 11 for Windows)

RESULTS

One hundred and twenty eight children (51 boys), aged 8 months to 14 years (mean 5±3.2 years) with polyps were included (Table 1). One hundred and twenty one children (94.53%) were found to have a solitary juvenile polyp (JP), while 3 (2.34%) had JPC. Among the JPC one polyp contained a focus of adenomatous hyperplasia. Three children (2.34%) aged 3, 5 and 10 years respectively, with a positive history of FAP had multiple adenomatous colonic polyps. One of them aged 10 years had malignant transformation of her largest polyp. This 10 year old girl had hepatoblastoma in infancy and her father had died at the age of 35 years from FAP-associated colonic adenocarcinoma. One child with Peutz-Jeghers syndrome, was diagnosed after the occurrence of small bowel intussusception.

The location of JP and the solitary Peutz-Jeghers polyp are shown in Table 2. FAP and JPC polyps were scattered throughout the colon. All polyps were pedunculated. All three children with JPC also had polyps located in the stomach and small intestine, without a positive family history of polyps.

On histologic evaluation, JP contained dilated, distorted glands with mucus and numerous polymorphonuclear cells, eosinophils, lymphocytes, plasma cells and histiocytes. Among the 128 children with colonic polyps, histology of surrounding and distal colonic mucosa was performed in 92 (including all children with FAP, JPC and Peutz-Jeghers). In 73 children (82.95%) a heavy eosinophilic infiltration in the juvenile polyp was noted (Figure 1 panel A). A significant eosinophilic infiltration in the lamina propria of colonic mucosa in the surrounding the polyp area as well as in distal areas (>20 eosinophils/high power field) was found in 67 (76.14%) children (Figure 1 panel B). All children with JPC also had mucosal eosinophilia, but no eosinophilia was found among the 3 children with FAP. Eosinophilic infiltration of the colonic lamina propria in the surrounding area as well as distally in stepwise analysis correlated significantly with patient's age, size of the polyp and colonic location of the polyps in the rectosigmoid. However, in multiple regression analysis (R2=0.49) the inverse correlation of eosinophilic infiltration with patient's age remained ($p<0.01$) and the positive correlation with the size of the polyp ($p<0.05$), but not with the location of the polyps in the colon.

Table 2. Location of 121 solitary colon polyps

Rectum	Sigmoid	Descending	Transverse	Ascending
69	21	23	5	3
56.56%	18.03%	18.85%	4.1%	2.46%

DISCUSSION

Our findings confirm previous studies that polyps in childhood are usually solitary, pedunculated, and juvenile in nature.[3,4] A significant number of our patients had polyps located proximal to the rectosigmoid region, as noted previously.[4] These polyps would be missed by sigmoidoscopy. Accordingly, due to the risk of malignant change, particularly in children with polyposis coli and adenomatous polyps,[5] routine colonoscopy should be considered as an initial investigation in children.

In children with a positive history of FAP, polyps were identified even during the first five years of life, a find-

Table 1. Colon polyps according to histology

Polyps	Total n (%)	Solitary JP n (%)	JPC n (%)	FAP n (%)	Peutz-Jeghers n (%)
Number of children	128	121 (94.53)	3 (2.34)	3 (2.34)	1 (0.78)
n of children with colonic biopsies	92	85	3	3	1
Eosinophils 20> HPF	67 (76.14)	64 (75.3)	3 (100)	0	0

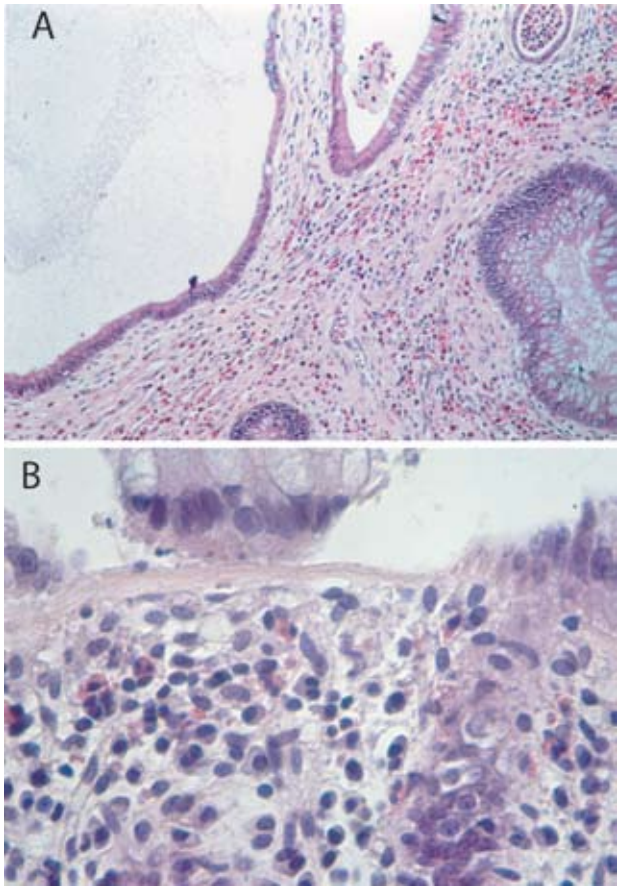

Figure 1. Eosiniphilic infiltration: Panel A. Juvenile polyp. Panel B. Colonic mucosa in the same patient.

ing that was also observed by other authors.[6] Among our patients, a 10-year-old child presented with cancer on the top of her largest polyp. Therefore earlier screening for children in families with FAP, even without symptoms, may be justified. Juvenile polyposis coli was found in 3 children, one of whom presented at the age of 8 months with severe bleeding. JPC has been associated with increased risk of colorectal cancer[7,8] accompanied with or without mutations.[7,9] JP are not premalignant,[10] although coexistent juvenile and adenomatous polyps in some patients can be found.[8]

In our study, increased eosinophilic infiltration was found within the polyp as well as in the colonic mucosa of patients with JP. Notably, mucosal eosinophilia was not identified in any of the 3 patients with FAP. Nevertheless, the number of children with FAP is too small to permit any statistical analysis between the two groups. In a study of adults, Moezzi et al.[11] found stromal eosinophilia in adenomas that decreased with progression through the adenocarcinoma sequence. In contrast, only 5% of hyperplastic polyps had any eosinophilic infiltration. Our results are in line with those of Kiparissi et al who also reported increased prevalence of mucosa eosinophilia in 8 out of 12 children with simultaneous colonic biopsies (67%) with JP or JPC[12] in a retrospective study of 13 children presenting with polyps over a ten year period. The advantage of our study is that it includes a large number of children having simultaneous colonic biopsies (92 children).

The pathogenesis of JP still remains obscure and there are several observations concerning the possible pathogenesis. Lipid-laden macrophages were identified in 83.3% of the biopsies near the polyp, but not distally from the polyp or from surrounding normal mucosa.[13] Iwamoto et al[14] found that in polyps from children with JP and JPC, nuclear beta-catenin accumulation is a consistent feature. Other factors may be related to innervation and blood vessels of the polyp or to inflammation of the colonic mucosa.[15] Another possible etiologic factor is allergy, a personal or family history of which was found in 11 of 13 patients studied by Alexander and associates.[16] There are no other published data suggestive of a high incidence of JP in allergic individuals, as is the case with nasal polyps, which are common in allergic patients.[17] However, in our study the fact that JP were characterised by the presence of an eosinophil-dominated inflammation (which is also operative in allergic inflammation), could be an indication of an allergic aetiology in the pathogenesis of colon JP. Several pro-inflammatory cytokines (GM-CSF, IL-3, IL-5) are increased in the tissue of nasal polyps.[18] The inflammatory cells themselves, especially eosinophils, are rich sources of many cytokines. Thus, colonic polyps can be looked upon as a type of self-perpetuating inflammatory process. IL-5 may play a key role in the pathophysiology of eosinophil dominated colon polyps and may further contribute to the creation of polyp tissue.

Eosinophilic infiltration of the colonic lamina propria correlated inversely with patient's age ($p<0.01$) -more frequent in young ages where allergy is also more common- and positively with the size of the polyp ($p<0.05$), but not with the location of the polyps in the colon. Similar results were presented by Nowicki et al[13] who found a colonic chicken-skin mucosa in 70% of children with JP but not in those with familial adenomatous polyposis or Peutz-Jegher syndrome. Nowicki et al[13] also noted a positive correlation of chicken skin mucosa with the size of polyps regardless of their location.

In conclusion, colon polyps in children were mainly juvenile, extend proximal to rectosigmoid in a large proportion, and may present as early as before the age of five years in children of families with FAP. Finally, the in-

creased eosinophilic infiltration of colonic mucosa found in a significant percentage of children with JP could be suggestive of a potential pathogenetic role for these cells. Further prospective studies with detailed clinical and laboratory evaluation of allergy, in addition to histological findings, could possibly provide additional data supporting the hypothesis of allergy as a contributing factor for the pathogenesis of juvenile polyps in children.

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